REMARKS

Applicant respectfully requests that the Examiner enter the above amendments for continued examination. These amendments are identical to those submitted with the Third Amendment dated 12 September 2003. The Third Amendment was submitted in response to the final Office Action dated 1 July 2003 within the three month shortened statutory period for such responses. Unfortunately, the Examiner did not respond to the Third Amendment with an Advisory Action (dated 8 January 2004) until after the six month statutory period for response to the final office action had expired. The application was therefore inadvertently allowed to go abandoned for failure to respond.

Below, Applicants reiterate their responses to the Examiner's rejections set forth in the final Office Action dated 1 July 2003 ("Office Action") and supplement those responses based on the Examiner's comments in the Advisory Action dated 8 January 2004 ("Advisory Action").

Summary of the Amendments

Claims 11 and 19 have been amended. Claims 11-24 are currently pending in the application.

Amendments to claims 11 and 19 further clarify that e-tag reporters have a charge and that a capture agent when bound to undigested electrophoretic probes forms a complex with a charge opposite to that of the e-tag reporters. Basis for the concept that e-tag reporters have charge can be found on page 15, lines 21-23 (where the term "mir" refers to the "mass identifying region" of a mobility modifier of an e-tag reporter, as explained on page 9, line 43, to page 10, line 5). Basis for the concept that released e-tag reporters have a charge opposite that of the capture agent-electrophoretic probe complex is on page 24, lines 9-13, and page 24, line 43, to page 25, line 3.

Claims 11 and 19 were further amended to change "non-oligomeric compound" back to the original claim language of "mobility modifier." Basis for this term is page 8, line 42, to page 9, line 5.

No new matter has been added by the amendments. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. 103

In paragraph 3 of the Office Action, the Examiner rejected claims 11-18 and 19-23 under 35 U.S.C. 103(a) as being unpatentable over Grossman (5,470,705) in view of Babon (5,851,770). The Examiner essentially reiterated her argument presented in the prior Office Action.

Applicants respectfully disagree, particularly in view of the amendments. Applicants submit that Babon is no longer applicable, as the use of the capture agent in Applicants' invention

to create a charge differential between undigested probe and released e-tag reporters is clearly different from the wash step disclosed by Babon. Applicants submit that neither Grossman nor Babon, either alone or together, disclose or suggest Applicants' invention as presently claimed, and therefore, respectfully request that the above rejection be withdrawn.

Applicants further disagree with the Examiner's assertion in the Advisory Action that "the teachings suggest that the probe of Grossman has a charge." Applicants request that the Examiner explain and support this assertion.

Applicants also disagree with the Examiner's assertion in the Advisory Action that Applicants' use of avidin to impart a charge to uncleaved probe is disclosed or suggested by Babon's use of avidin. Babon discloses a conventional purification step using avidin *or streptavidin* that is attached to a solid phase support to capture a biotinylated target stranded (see for example, Figs. 2, 5, and 6; col. 3, line 34-35; col. 10, line 32; and col. 8, lines 27-37)(emphasis added). It is well known that avidin (pI $\approx$ 10-10.5) is a positively charged protein and the streptavidin (pI $\approx$ 5) has little or no charge at neutral pH. Applicants' invention specifically calls for a capture agent that will change the charge of a probe. Not only does Babon fail to disclose or suggest the significance of a charged capture agent in an assay, but it teaches away from the use of a charged capture agent by suggesting the use of a capture agent without a charge.

Moreover, Babon discloses the use of a capture agent only in conjunction with a solid support. This is because Babon teaches a physical wash step (see col. 8, lines 27-37, and Figs.) prior to cleavage with an enzyme that recognizes mismatches and analysis of fragments by electrophoresis. This teaches away from Applicants' use of a charged capture agent to exclude uncleaved probe from being electrophoretically separated with released etag reporters.

In paragraph 4 of the Office Action, the Examiner rejected claim 24 under 35 U.S.C. 103(a) as being unpatentable over Grossman (cited above) in view of Babon (cited above) and further in view of Ullman (U.S. patent 6,251,581B1). The Examiner applied Grossman and Babon as above and further argued that the specific structures recited in claim 29 are disclosed by the chemiluminescent compounds of Ullman.

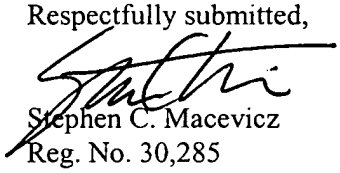
Applicants respectfully disagree, particularly in view of the amendments. First, as stated above, Applicants submit that the disclosure of Babon is no longer applicable. Second, although Ullman discloses compounds similar to those recited in claim 24, the *compositions of Applicants' invention comprise pluralities of such compounds that form distinct peaks in an electropherogram upon electrophoretic separation.* Such compositions are neither disclosed nor suggested by Ullman. In fact, Ullman teaches away from such compositions because his objective is to provide a homogeneous assay based solely on optical (chemiluminescent) detection without any separation of the optically detected molecules. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Applicants' respectfully submit that in the Advisory Action the Examiner has engaged in an exercise of hindsight reconstruction of Applicants' invention. The invention of claim 24 includes all the limitations of the claims it depends from, which includes a recitation of a *plurality* of electrophoretic probes from which the structures of claim 24 are derived by cleavage, and the limitation that the structures all be separable from one another by electrophoresis. Applicants submit that none of the cited references disclose or suggest these limitations.

In view of the above, Applicants submit that the claims as written fully satisfy the requirements of Title 35 of the U.S. Code, and respectfully request that the rejections thereunder be withdrawn and that the claims be allowed and the application quickly passed to issue.

If any additional time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account **50-2266**.

Respectfully submitted,



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